ENVIRONMENTAL PROTECTION AGENCY
Washington, D.C. 20460

OFFICE OF PESTICIDE
PROGRAMS
Health Effects Division

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MEMORANDUM

SUBJECT: ***ETHYL PARATHION*** **- REEVALUATION** of Toxicology Endpoint Selection; Report of the Hazard Identification Assessment Review Committee

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THROUGH: Pauline Wagner, Co-Chair
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TO: Richard Griffin, Risk Assessor
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PC Code: 057501

On August 12, 1999 the Health Effects Division's Hazard Identification Assessment Review Committee (HIARC) reevaluated the endpoints selected for dietary and non-dietary risk assessment for ethyl parathion because the registrant requested reconsideration in response to preliminary risk assessment release to the public docket on January 15, 1999 (FR Vol. No. 10; OPP-34171) . The HIARC's conclusions are presented in this report.

Committee Members in Attendance

Members present: William Burnam, Pam Hurley, Susan Makris, Nicole Paquette, Kathleen Raffaele, David Anderson, Virginia Dobozy, Pauline Wagner, Jess Rowland, PV Shah, Mike Ioannou, and Brenda Tarplee (Executive Secretary).

Data was presented by Nicole Paquette of Reregistration Branch 2.

Also present: Robert Zendzian, SAB.

Data Presentation and Report Preparation:	Nicole Paquette Toxicologist

I. INTRODUCTION

Previously, the Committee had selected the acute oral neurotoxicity study for use in acute dietary risk assessment (HIARC Report, 4/27/98). Effects seen at 2.5 mg/kg in male and female rats in this study included plasma, red blood cell (RBC) and brain cholinesterase inhibition and changes in functional observation battery and motor activity in females. The NOAEL from this study was set at 0.025 mg/kg in male rats and 0.5 mg/kg for female rats. The male rat NOAEL of 0.025 mg/kg was selected instead of the female rat NOAEL of 0.5 mg/kg for the acute dietary risk assessment based on the effects seen at the next highest dose in male rats (LOAEL = 2.5 mg/kg). Because the mid and low doses used in this study in male rats differed by a factor of 100, the registrant requested reconsideration that the NOAEL from the female rats (0.5 mg/kg) be used for the acute dietary risk assessment.

On August 12, 1999, the Committee evaluated available data for ethyl parathion, and agreed with the registrant that the NOAEL for female rats (the most sensitive sex) was 0.5 mg/kg. However, there was an 8% decrease in red blood cell cholinesterase activity in this group compared to control which could not be dismissed. While this inhibition was slight and not statistically significant there was support of a similar effect in a 1991 pilot study (MRID 41834501), in which female rats (2 rats/dose) given 0.25 mg/kg and 0.50 mg/kg had approximately 34% and 42% decrease in plasma cholinesterase, respectively, and approximately 6 % and 8% decrease in red blood cell cholinesterase, respectively, after 1 day of treatment. The Committee had less confidence in the NOAEL of 0.5 mg/kg in female rats in light of the pilot study data and the slight decrease in red blood cell cholinesterase in the selected acute neurotoxicity study. Furthermore, while the Committee acknowledges that there was no dose between 0.025 mg/kg and 2.5 mg/kg in male rats, there was still uncertainty about the effects which might occur at doses less than 2.5 mg/kg thus making a poor dose response assessment in male rats. For these reasons, the Committee had greater confidence that the NOAEL was below 0.5 mg/kg, and selected the NOAEL of 0.025 mg/kg for the acute dietary risk assessment endpoint.

Although the Committee recognized that the use of this study for acute dietary risk assessment with a NOAEL of 0.025 mg/kg was conservative, the Committee believed that the endpoint selected would not underestimate the risk for a single exposure.

II. HAZARD ASSESSMENT

A. Acute RfD

Study Selected: Acute Oral Neurotoxicity §81-8

MRID No.: 43117901

Executive Summary: Male and female Sprague Dawley rats (10/sex/dose) were orally gavaged once with ethyl parathion (96.2%) at doses of 0 (corn oil), 0.025, 2.5, 10.0 mg/kg for males and

0, 0.025, 0.5, 2.5 mg/kg for females. Neurobehavioral effects (FOB and motor activity) on all animals were evaluated prior to dosing on day 0, at the peak time-of-effect (4 hr after dosing) and on days 7 and 14. Cholinesterase (ChE) determinations were conducted on blood on all animals 2 days prior to dosing; blood and brain ChE were determined 4-hr after dosing (Day 0), and on day 14 (5 rats/sex/dose/time point). Neuropathological examinations were carried out at terminal sacrifice (day 14) on 6 rats/sex/dose.

Two high dose (10.0 mg/kg) male rats died on the day of dosing. Clinical signs and FOB evaluations consistent with acute cholinergic toxicity were noted in all surviving male rats at the highest dose and one high dose female. Hypoactivity, labored breathing, rough coat, chromodacryorrhea, urine stains, muscle fasciculations, tremors, salivation were observed in all high dose males (10 mg/kg) and one high dose female (2.5 mg/kg). Evaluation of the FOB/motor activity data at the 4 hour testing interval revealed a treatment-related increase in abnormal observations in the high dose male and female rats for home cage/hand held, open field, response and performance data. Recovery from cholinergic effects was complete for the majority of high dose male rats (6/8) and all female rats by day 14.

There were statistically significant ($p \leq 0.5$) depressions of plasma and RBC cholinesterase activity at the 4 hour peak time-of-effect in male rats given 10mg/kg (↓18%) and 2.5 mg/kg (↓25% of control) and female rats given 2.5 mg/kg (↓39%). Partial to full recovery was observed at 14 days post dose, however, male rats given 10 mg/kg still had statistical significant ($P \leq 0.5$) reduction (↓40%) in RBC ChE activity.

The highest dose tested in males (10 mg/kg) and females (2.5 mg/kg) produced statistically significantly ($p<0.5$) decreased brain ChE activity (↓24 % and ↓30%, respectively) in all measured areas of the brain. By day 14, all brain ChE activity returned to normal except the brainstem in male rats given 10 mg/kg (↓33%). There were no treatment related effects noted in the neuropathological examination.

Based on the results of this study, the neurobehavioral NOAEL is 2.5 mg/kg for males and 0.5 mg/kg for females; the LOAEL is 10 mg/kg for males and 2.5 mg/kg for females as evidenced by the abnormal FOB and clinical signs of cholinergic toxicity.

The NOAEL for plasma and RBC cholinesterase inhibition is 0.025 mg/kg for male and0.5 mg/kg for female rats; the LOAEL is 2.5 mg/kg for both male rats and 2.5 mg/kg for female rats. For brain ChE inhibition the LOAEL is 10 mg/kg (HDT) for male rats and 2.5 mg/kg (HDT) for female rats; the NOAEL is 2.5 mg/kg, and 0.5 mg/kg, respectively.

Dose and Endpoint for Establishing RfD: NOAEL = 0.025 mg/kg based on plasma and RBC cholinesterase inhibition occurring at 2.5 mg/kg for male rats.

Comments about Study/Endpoint: This is a well conducted study and is very appropriate for use in acute dietary risk assessment since the endpoint (plasma and RBC cholinesterase inhibition)

was measured after a single oral dose at 4 hours on the day of treatment (i.e., exposure period of concern). In a pilot study, it was determined that female rats were approximately 4 times more sensitive to ethyl parathion toxicity compared to male rats, therefore, different doses were used for each sex. In addition, the dose response gradient for this chemical is steep; 2 male rats at 10.0 mg/kg died on day of dosing and at Day 14 male rats given 10 mg/kg still had statistical significant decreased RBC & brain ChE and some male rats had not fully recovered from cholinergic signs. Although the decrease in RBC cholinesterase in female given 0.5 mg/kg was not statistically significant the dose related effect may indicate a biological significance. This is supported by a pilot study conducted for a subchronic feeding study in rats (MRID 41834501) in which two female rats given 0.50 mg/kg bw had an approximate 42% decrease in plasma cholinesterase and an 8% decrease in RBC cholinesterase compared to control group following 1 day exposure to ethyl parathion. The next lowest dose (0.25 mg/kg bw) showed a 34 % decrease in plasma cholinesterase and an 6% decrease in RBC cholinesterase. HED acknowledges that there is no dose between 0.025 mg/kg and 0.5 mg/kg in female rats and 0.025 mg/kg and 2.5 mg/kg in males but considers the acute neurotoxicity study a well conducted study and appropriate for use in the acute dietary risk assessment.

Uncertainty Factor (UF): 100 (10x for interspecies extrapolation and 10x for intraspecies variability).

$$\textbf{Acute RfD} = \frac{0.025 \text{ mg/kg}}{100 \text{ (UF)}} \text{ (NOAEL)} = \textbf{~~0.0003~~ 0.00025* mg/kg/day}$$

* Corrected rounding error; 09/07/99 BSTarplee.

B. CHRONIC REFERENCE DOSE

The Committee reaffirmed the dose and endpoint previously selected for the chronic dietary risk assessment.

Study Selected: One year feeding study in dogs §83-1

MRID No.: Acc# 24664243

Executive Summary: Four groups of beagle dogs (8/sex/dose) were administered ethyl parathion (95.5%) in the diet at doses of 0, 0.01, 0.03, or 0.10 mg/kg/day for 12 months. Clinical signs were determined daily and body weight and food consumption were determined weekly. Hematology and clinical chemistries were performed prior to dosing, monthly thereafter and at termination. Plasma and RBC cholinesterase determinations were made twice before dosing, at months 2, 4 and 12. Brain cholinesterase activity was performed along with gross and microscopic examination of selected tissues at termination. Urinalysis was performed prior to dosing and at months 3 and 12.

All dogs survived the entire study. There were no compound-related clinical signs of toxicity, at any time observed. There were no effects on body weight, body weight gain, food

consumption, clinical chemistries, urinalysis, organ weights or histopathology.

There were dose-related statistical significant ($p<0.05$) decreases in plasma and RBC cholinesterase activity in both male and female dogs, compared to control animals. Throughout the study, plasma and RBC cholinesterase activity were sporatically but significantly depressed at all dose levels, at the 2 and 12 month period but not the 4 month interval. By the end of 12 months, however, plasma cholinesterase activity was significantly depressed for both sexes (males: 73-46% of control; females: 85-34% of control). RBC cholinesterase activity was also statistically significantly reduced at all doses (males: 78-58% of control; females: 86-63% of control). Brain cholinesterase was only statistically significantly reduced in female dogs given 0.03 mg/kg (mid-dose) , compared to control.

The LOAEL was 0.01 mg/kg (LDT) based on decreased plasma and RBC cholinesterase activity in both male and female dogs; a NOAEL was not established.

Dose and Endpoint for Establishing RfD: LOAEL = 0.01 mg/kg based on decreased plasma and RBC cholinesterase activity in both sexes.

Uncertainty Factor(s): An uncertainty factor of 100 was applied to account for both interspecies extrapolation and intraspecies variability. An additional uncertainty factor of 3 was applied because of the use of a LOAEL (i.e., lack of a NOAEL in critical study). Although a NOAEL was not established in this study, the Committee determined that an additional factor of 3 was adequate because the study was well conducted and there are sufficient data from subchronic and chronic duration studies in the same species and other species which support cholinesterase inhibition as the critical toxic effect.

$$\textbf{Chronic RfD} = \frac{\text{0.01 mg/kg/day (LOAEL)}}{\text{300 (UF)}} = \textbf{0.000033 mg/kg/day}$$

Comments about Study/Endpoint: The results of a 6-month study in dogs (MRID 41836601) support the results of the 1-year study in dogs and is used as support for the critical study. The RfD of 0.000033 mg/kg/day (see calculation above) is comparable to the RfD (0.000024 mg/kg/day) that could have been derived from using a NOAEL of 0.0024 mg/kg/day established in the 6 month rat study and an UF of 100 (0.0024 mg/kg/day ÷ 100 = 0.000024 mg/kg/day). The HIARC selected the 1-year study with the LOAEL instead of the 6-month study with a NOAEL, because of the longer (1-year) duration which is appropriate for establishing the RfD.

C. OCCUPATIONAL EXPOSURE

1. Dermal Absorption

No dermal absorption studies are available. Therefore, the Committee selected the default value of 100% (assume equivalent dermal and oral absorption). This 100% default assumption is

supported by similar toxicity which results at similar doses in acute oral and dermal studies in several species (rat oral LD_{50}=3 mg/kg, rat dermal LD_{50}= 6.8 mg/kg; rabbit oral LD_{50}=10 mg/kg, rabbit dermal LD_{50}= 15 mg/kg; guinea pig oral LD_{50} =8 mg/kg, guinea pig dermal LD_{50}= 45 mg/kg; mouse oral LD_{50}=5 mg/kg, mouse dermal LD_{50}= 19 mg/kg). Also, the dermal absorption estimation was based on the physical and chemical properties of ethyl parathion and the use of structure activity relationship to its homolog, methyl parathion and includes data supporting a 100% dermal absorption factor (HIARC Report #013270, 2/24/99).

2. Short Term Dermal Exposure

The Committee also considered the registrant's proposal that the acute dermal toxicity study (MRID 40814002) should be used for the short term dermal exposure risk assessment. The current short term dermal exposure toxicity endpoint (NOAEL = 0.025 mg/kg), is based on the plasma and red blood cell cholinesterase inhibition in male rats at 2.5 mg/kg in an acute neurotoxicity study. The Committee agreed that the endpoint from the acute neurotoxicity study might not be appropriate for the short term exposure assessment. The NOAEL from the acute dermal toxicity study in rats was 0.45 mg/kg based on decreased plasma cholinesterase (10%) activity in female rats at 0.68 mg/kg (LOAEL). While this endpoint might be appropriate for a one-day dermal exposure period, the Committee believed that the use of this study would underestimated the risk for any exposure period longer than 1 day. For this reason, the Committee selected the NOAEL of 0.01 mg/kg bw/day from a six month dog toxicity study (MRID 41836601) in which plasma cholinesterase was markedly decreased in male and female dogs at the <u>one week time period</u> by approximately 84% and 79%, respectively, at 0.8 mg/kg bw/day (LOAEL) compared to control or pretreatment values. No other subchronic rat or dog study was available that measured cholinesterase activity at the one week time period.

<u>Study Selected</u>: 6-month feeding study in dogs

<u>MRID:</u> 41836601

<u>Dose and Endpoint for Risk Assessment:</u> NOAEL = 0.01mg/kg based on markedly decreased plasma cholinesterase activity in male and female dogs at the one week time measurement at 0.8 mg/kg bw (LOAEL).

<u>Comments about Endpoint:</u> Although there were no other one week time period measurement of cholinesterase activity, there was a 90-day oral toxicity study in female rats (MRID 41834501) in which red blood cell cholinesterase activity was statistically significantly decreased at 0.4 and 4.0 mg/kg bw/day by Week 2 through termination. Plasma cholinesterase was also reduced to 75% of control at Week 2, but was not statistically significant. The NOAEL in this study was 0.04 mg/kg bw/day which supports the same toxicity endpoint (NOAEL/LOAEL) in the 6-month dog toxicity study at the one week interim measurement.

3. Intermediate Term Dermal Exposure

The Committee reaffirmed the selection of the toxicity endpoint from the 6 month dog toxicity study (MRID 41836601) for the intermediate term dermal exposure risk assessment.

Study Selected: 6 Month Oral Toxicity Study in Dogs §83-1b

MRID No.: 41836601

Executive Summary: Beagle dogs (5/sex/dose) were orally dosed by capsule with ethyl parathion (98%) at 0 (corn oil in gelatin capsules), 0.0024 (0.002), 0.0079 (0.01), or 0.7937 (0.8) mg/kg/day for six months. The following parameters were evaluated: twice daily observations; pretest physical examinations and body weights and then weekly thereafter; food consumption pretest and weekly thereafter; plasma and red blood cell (RBC) cholinesterase activity pretest, and weeks 1, 6, 14, 20 and 26. Brain, retina and ocular muscle cholinesterase activity were determined at termination. Routine opthalmoscopic examinations, slit lamp examinations were performed at pretest, months 3 and 6; electroretinograms, eye refraction, and intraocular pressure determinations were performed at pretest, months 1, 3 and 6. Histopathology of the retina, optic nerve, muscle and ciliary body was conducted at termination.

There was no effect on body weight gain in male dogs at any dose; in the high dose (0.8 mg/kg) female dogs, there were decreases in body weight gain throughout the study which may have been treatment related. There were no effects on food consumption at any dose in either sex during the study.

Plasma cholinesterase activity was reduced as early as Week 1 and markedly reduced by Week 6 and throughout the rest of the study in both male and female dogs given 0.01 and 0.8 mg/kg. Compared to pretreatment values, plasma cholinesterase activity in male and female dogs given 0.01 mg/kg was reduced by 20% and 25%, respectively. The highest dose (0.8 mg/kg) decreased plasma cholinesterase levels in male dogs by 84% (16% of pretreatment value) and in female dogs by 82%, compared to pretreatment values. There was a slight reduction in RBC cholinesterase activity in both male and female dogs given 0.8 mg/kg; 18% for both sexes compared to pretreatment values. Brain cholinesterase activity was statistically significantly decreased in male rats given 0.8 mg/kg (HDT).

The LOAEL for systemic toxicity was 0.8 based on decreased body weight gain in female dogs during the whole study; the NOAEL was 0.01 mg/kg. The LOAEL for plasma ChE inhibition in male and female dogs was 0.01 mg/kg; the NOAEL was 0.002 mg/kg. The LOAEL for RBC and brain ChE inhibition was 0.8 mg/kg; the NOAEL was 0.01 mg/kg.

Dose/Endpoint for Risk Assessment: NOAEL = 0.002 mg/kg based on the markedly reduced plasma ChE in male and female dogs by Week 6 and throughout the study at 0.01 mg/kg (LOAEL).

Comments about Study/Endpoint: The corroborating effects of cholinesterase inhibition associated with ethyl parathion were noted in several other intermediate term (subchronic) studies at similar doses in other species. In a 3 month oral toxicity dog study, (MRID# 71670), groups of 4 male and 4 female beagle dogs were given dietary ethyl parathion (99.4%) at doses of 0, 0.3, 1.0 or 3.0 mg/kg. The only treatment related effect was statistically significant inhibition of plasma cholinesterase at all doses in both sexes at Weeks 6 and 13 and statistically significant inhibition of RBC ChE in females at all doses at Weeks 13. Based on plasma and RBC ChE

inhibition, the LOAEL was the lowest dose tested, 0.3 mg/kg for both sexes and no NOAEL was established.

Although the dog is the most sensitive species, plasma, RBC and brain cholinesterase inhibition was the critical toxic effect in several subchronic oral studies in rats. In a subchronic neurotoxicity study (MRID# 43491501), female rats fed dietary levels of 0.05, 1.25 or 2.5 mg/kg, and male rats fed 0.05, 2.5 or 5.0 mg/kg for 13 weeks, there was a statistically significant decrease in RBC cholinesterase activity in both sexes at 0.05 mg/kg and no NOAEL could be established.

In another 13-week feed study (MRID# 41834501), female rats (the most sensitive sex) were given 0.04, 0.4 or 4.0 mg/kg of ethyl parathion. The NOAEL was 0.04 mg/kg based on markedly reduced RBC cholinesterase activity at 0.4 mg/kg (LOAEL) at Week 2 of study.

4. Long-term Dermal Exposure

Based on the current use pattern, no long-term dermal exposure is expected to occur.

5. Inhalation Exposure (Short and Intermediate Term)

Based on the high acute toxicity (LC_{50}= 0.084 mg/L) and the use pattern (0.5 - 1.0 lbs a.i/acre) there is considerable concern for potential inhalation exposure or risk. Inhalation of ethyl parathion vapor and/or aerosol leads to rapid absorption with imminent risk of respiratory failure. Therefore, the HIARC selected the oral dose for inhalation risk assessment. Short and intermediate term aggregate risk assessment should follow the route-to-route extrapolation as below:

Step I. The inhalation exposure component (i.e. µg a.i /day) using 100% absorption rate should be converted to an equivalent oral dose (mg/kg/day).

Step II. The dermal exposure component (mg/kg/day) using a 100% dermal absorption rate should be converted to an equivalent oral dose. This dose should then be combined with the oral dose in Step I.

Step III. The combined dose from Step II should then be compared to the oral NOAEL's of 0.01 mg/kg/day for short term and 0.002 mg/kg/day for intermediate term exposures to estimate the combined risk.

III. RECOMMENDATION OF THE FQPA FACTOR

The FQPA Safety Factor Committee met on June 15 and 16, 1998 to evaluate the hazard and exposure data for ethyl parathion and recommend application of the FQPA Safety Factor (as required by Food Quality Protection Act of August 3, 1996) to ensure the protection of infants and children from exposure to these pesticides.

The FQPA Safety Factor Committee has determined that the FQPA safety factor can be removed for ethyl parathion. For details, refer to the FQPA Safety Committee Report dated August 6, 1998.

IV. HAZARD CHARACTERIZATION

Ethyl Parathion is among the most highly toxic organophosphorus insecticide registered and is a potent inhibitor of acetylcholinesterase (AChE). Acute lethality occurs in mammals at low doses regardless of route of exposure. Toxic symptoms are largely caused by the inhibition of cholinesterase in the peripheral and central nervous system. In acute oral toxicity studies, female rats are more sensitive to the toxic and lethal effects of ethyl parathion compared to male rats. As with all sulfur-containing organophosphates, to produce toxicity, ethyl parathion must first undergo metabolic activation to its biological active oxygen analog, paraoxon. Symptoms leading up to death are consistent with cholinergic overstimulation and include, headache, weakness, blurred vision, pin-point pupils, sweating, watering of eyes, drooling or frothing of the mouth, vomiting, tightness in the chest, labored breathing, muscle spasms, convulsions and coma. In severe poisonings, death is primarily due to respiratory arrest from paralysis of the respiratory muscles.

Dogs are the most sensitive species to cholinesterase inhibition in repeated dose studies. In subchronic and chronic studies in dogs, plasma, RBC and brain cholinesterase inhibition are the predominant critical effect occurring at relatively low doses. On the other hand, rats manifests other toxic effects, apart from the cholinergic effects. In a subchronic dietary study, female rats fed ethyl parathion also had increased mortality rates and decreased body weights and male rats had decreased body weights in addition to cholinesterase inhibition. In a chronic study, female rats had a higher mortality rate, developed anemia and retinal atrophy and degeneration and male rats developed severe myelin sheath degeneration of the sciatic nerve. These longer term toxicities occurred at doses which were greater than those lower doses which inhibited cholinesterase activity.

Ethyl parathion is not a developmental toxicant and has no effect on reproduction. In developmental toxicity studies in rats and rabbits and a two-generation reproduction study there was no evidence of malformations or decreases in the number of pups and/or litter or surviving offspring.

Ethyl Parathion was classified as a Group C (possible human carcinogen) with a RfD approach for human risk characterization. This classification is based on the increased adrenal cortical tumors in male and female Osborne-Mendel rats and possible trends for thyroid follicular adenomas and pancreatic islet cell carcinomas in male rats in the same study. No evidence of mutagenicity was seen in any study.

The metabolism of ethyl parathion involves an oxidative desulfuration step (that significantly enhances the anticholinesterase properties) to its oxygen analog, paraoxon. Further oxidative 0-deethylation occurs to produce hydrolysis products which are excreted almost entirely in the urine.

V. SUMMARY OF TOXICOLOGY ENDPOINT SELECTION

The doses and toxicological endpoints selected for various exposure scenarios are summarized below:

EXPOSURE SCENARIO	DOSE (mg/kg/day)	ENDPOINT	STUDY
Acute Dietary	NOAEL=0.025 UF = 100	Plasma and RBC ChE Inhibition in males at 2.5 mg/kg	Acute Oral Neurotoxicity in Rats
	Acute RfD = ~~0.0003~~ 0.00025* mg/kg/day		
Chronic Dietary	LOAEL=0.01 UF = 300	Plasma and RBC ChE Inhibition in both male and female dogs at 0.1 mg/kg	Chronic Toxicity -Dog
		Chronic RfD = 0.00003 mg/kg/day	
Short-Term (Dermal)	Oral NOAEL=0.01	Plasma ChE Inhibition in male and female dogs after 1 week of dosing at 0.8 mg/kg bw/day	6-Month Oral Toxicity Study in Dogs
Intermediate-Term (Dermal)	Oral NOAEL=0.002	Plasma and RBC ChE Inhibition in both male and female dogs at 0.008 (0.01) mg/kg	6 Month Oral Toxicity -Dog
Long-Term (Dermal)	None	The use pattern and exposure scenario does not indicate a need for long term risk assessment	
Short Term (Inhalation)	Oral NOAEL=0.01	Plasma ChE Inhibition in male and female dogs after 1 week of dosing at 0.8 mg/kg bw/day	6-Month Oral Toxicity Study in Dogs
Intermediate Term (Inhalation)	Oral NOAEL=0.002	Plasma and RBC ChE Inhibition in both male and female dogs at 0.008 (0.01) mg/kg	6 Month Oral Toxicity -Dog
Long Term (Inhalation)	NONE	The use pattern and exposure scenario does not indicate a need for long term risk assessment	

* Corrected rounding error; 09/07/99 BSTarplee.